

GRANULAR TUBERCULOUS CONJUNCTIVITIS TREATED BY INSTILLATIONS OF TUBERCULIN.¹

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THE following case is reported to call attention to a method of treating a subacute tuberculous condition of the conjunctiva which, so far as I know, has not been previously employed except by Ellis and Gay,² whose article came to my notice after treatment had been inaugurated. This case also demonstrates the beneficial effects of controllable focal reactions produced by tuberculin on tuberculous tissues.

CASE HISTORY. C. S., male, clerk in a shipping office, aged twenty-three years. Has had symptoms of pulmonary tuberculosis since the early summer of 1916. Examination of the chest shows a marked infiltration of the right upper and middle lobes and to a lesser extent in the lower part of the left upper lobe. Tubercle bacilli were present in the sputum. There is some involvement of the larynx, with marked hoarseness, for the past eighteen months. Although he has had hemoptysis on several occasions, the course of the disease has been one of slow improvement. In May, 1917, the patient first noticed that the left eye was inflamed, and pain, which was severe enough to keep him awake at nights, was felt in the eye and forehead. Reading increased the pain; there was little discharge and the lids were never glued together in the morning; there was no photophobia; vision was said to be somewhat blurred; there was no fever associated with this condition. I first saw the patient early in August, 1917, at which time the inner part of the left bulbar conjunctiva and the part below the cornea were covered with pale, sluggish, trachoma-like granulations, which were also present on the conjunctival surfaces of both eyelids, especially the lower. There was some injection of the conjunctival vessels; no ulceration was present and there were no definite tubercles. The cornea was not involved. There was no enlargement of the preauricular lymph nodes. A small amount of mucoid secretion was present, but this was not marked. Cultures from the conjunctival sac revealed staphylococci and a large Gram-positive bacillus. The condition failed to respond to the ordinary eye washes and astringents. With the approval of Dr. E. R. Baldwin, who agreed that the condition was probably tuberculous, on August 17, 2 drops of a 0.00001 dilution of O. T. were instilled directly into the left conjunctival sac. No reaction followed this, and on August 21, 2 drops of 0.0001 O. T. were instilled likewise without reaction. On August 24, 2 drops of

¹ Read before the American Climatological and Clinical Association, June 5, 1918.

² Lancet, August 4, 1917, No. 4901, cxviii, 156.

0.001 O. T. were instilled and 2 drops of this same solution were again introduced four days later, no reaction following in either case. On September 6, 2 drops of 1 per cent. solution of O. T. were instilled into the left conjunctival sac, and this was followed by a sharp local reaction, characterized by increase in the pain during the evening of the day on which the instillation was made by marked increase in the amount of secretion, which became thick and yellowish, causing the eyelids to stick together. There was marked dilatation of all the conjunctival vessels and swelling of the conjunctiva and lids. This reaction passed off within forty-eight hours, by the end of which time the conjunctiva appeared clearer and the granulations were smaller than before the treatment. Ten days later a similar dose, namely, 2 drops of 1 per cent. solution, was instilled and almost immediately a dilatation of the conjunctival vessels could be seen and a sharp reaction followed, as in the former instance. This treatment was continued for six doses, at about ten-day intervals, making in all eight treatments, with reactions, after which the conjunctiva showed little evidence of disease. All symptoms had entirely disappeared, and at the time of writing the only evidence of previous disease is a few fine granulations and slight reddening of the bulbar conjunctiva at the extreme inner canthus. The palpebral conjunctiva is clear, but there seems to be some thickening, as the palpebral slit is slightly narrower than that of the opposite eye and the patient is not able to open the affected eye quite as widely as the right. The lung condition and throat disease have been quiescent during the treatment and have not been affected by the reactions. The patient is now doing light office work for the first time in two years.

Discussion. Tuberculosis of the conjunctiva is one of the rarer localizations of this infection and may occur in the form of (1) ulcers, including lupus; (2) miliary tubercles; (3) granulations, including phlyctenules; (4) pedunculated tumors. A full description of these various forms and a general discussion of the subject of tuberculosis of the conjunctiva has been given by Eyres³ in the Hunterian Lecture of 1912. Although tubercle bacilli were not demonstrated and no histological study was made of the granulations, as I did not care to excise any of the tissue for fear an ulcer would result at the site of the wound if bacilli were present in the granulations, the case here reported is in all probability one of tuberculosis of the conjunctiva. The clinical features in this case closely resembled the picture seen in Parinaud's conjunctivitis, except for the absence of enlargement of the preauricular lymph nodes, which is usually present in this disease. Möllers⁴ has reported 2 cases of Parinaud's conjunctivitis, in which he demonstrated the presence of tubercle bacilli in the granulations by animal inoculation, and in this report quotes the

³ *Lancet*, May 18, 1912, No. 4629, clxxxii, 1319.

⁴ *Veröffentlichungen der R. Koehsche Stiftung*, Heft 4, 1913.

previous work of Wessely and others, who had proved the tuberculous nature of this disease. In this case the ordinary local tuberculin tests would not have assisted in diagnosis, as a positive reaction would have been obtained from the infection in the lungs, and although a subcutaneous test might have produced a focal conjunctival reaction, its use was contraindicated, owing to the danger of a general reaction on the pulmonary condition. The characteristics of the conjunctival lesion, the resistance to ordinary treatment, the presence of extensive tuberculosis elsewhere in the body and the marked focal reaction to tuberculin, followed by recovery, appear to justify the conclusion that the condition was a tuberculous one.

There has been much discussion and confusion as to the nature of the tuberculin reaction and as to how tuberculin aids in the cure of tuberculosis. Certain facts about the action of tuberculin are known, and a great many have been assumed without proof or sufficient experimental confirmation. Among these latter may be mentioned the production of antibodies of one kind or another in the serum and the development of a condition akin to anaphylaxis. The first of the known facts is that tuberculin has not a primary toxic action, even when used in enormous doses, on normal animals or persons, that is, on animals free from tuberculosis. Hamburger² reports having given 500 mg. of O. T. subcutaneously, without producing any general effects, to a child, which had failed to react to a previous skin test and which could, therefore, be considered non-tuberculous. Krause, working in the Saranac Laboratory, administered 25 c.c. of watery extract of tubercle bacilli intravenously to a normal guinea-pig without ill-effects, except for a watery diarrhea lasting a few days and caused by the rapid increase in the amount of fluid in the body. It may therefore be repeated that tuberculin has no deleterious effect on normal animals. Secondly, the presence of anatomic tubercle alters the body in some way so that all the tissues acquire a hypersensitiveness to tuberculin. This allergic condition or hypersensitiveness disappears when the tuberculous focus is completely healed or removed from the body. Thirdly, tuberculin acts specifically on tuberculous foci themselves, causing an acute inflammation in and around them. These focal reactions may be seen in experimental animals, killed during a general tuberculin reaction, and also are observed clinically in cases of tuberculosis where the disease is capable of direct observation, as in laryngeal and skin tuberculosis. The hyperemia accompanying this focal reaction permits of a dissemination of substances whose nature is not yet definitely known, and the entrance of these substances into the systemic circulation produces what is known as the general tuberculin reaction. The focal reaction thus produced by tuberculin may be a source of danger if the reaction is so great as to

² München. med. Wchnschr., 9 Juni, 1908, No. 23, I, 1220.

lead to a dissemination of bacilli to previously healthy tissues. On the other hand, if these reactions are slight and controllable the result of the inflammation is a tendency to walling off of the diseased foci by fibrosis, which is what we know as healing. The immediate object of tuberculin treatment should therefore be the production of slight and controllable reaction around the focus of disease. While this is simple when thus stated, it is not so simple in practice, particularly in pulmonary cases, for we are here dealing with a multiplicity of small foci in varying stages of development, from early and recent cellular tubercles to older, more or less fibrous or caseonecrotic tubercles, which will be influenced differently by the same dose of tuberculin. If we add to this difficulty the fact that our methods of observing and estimating the results clinically are relatively coarse and depend chiefly on the patient's subjective symptoms, the difficulties and chances of error in judging the effects of our dosage are apparent.

The case here reported shows the beneficial results of such focal reactions, and a clearing up of the granulations was noticeable after each reaction. In this case it would have been unwise to give tuberculin subcutaneously on account of the extent of the disease in the lungs, but fortunately the location of the disease in the conjunctiva permitted of direct application and direct observation of the results. As the reaction was purely local, the beneficial results cannot be attributed to changes in the serum nor to an alteration in the so-called general resistance of the system, but must be ascribed to local tissue changes. Whether a non-specific irritant, which would have produced an inflammatory reaction, would have brought about similar beneficial results cannot be stated or denied, as it was not tried, but the use of jequirity in granular eye conditions is an old method and might give grounds for the belief that this or other non-specific inflammation-producing remedy might have been equally efficacious.

STUDY OF AN UNUSUAL GLYCOSURIA.

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THERE has previously been reported a type of glycosuria in which while glucose was constantly excreted there were no symptoms of diabetes, the amount of sugar in the urine bore little or no relation to the amount of carbohydrate ingested and the blood sugar was normal. Klemperer,¹ who first noted this condition, found it associated with

¹ Verhändl. der Ver. f. inn. Med., Berlin, 1896, xvi, 67.